Preterm Birth/Low Birth Weight and Markers Reflective of Wealth in Adulthood: A Meta-analysis

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abstract

CONTEXT: Preterm birth and/or low birth weight (PT/LBW) increases the risk of cognitive deficits, which suggests an association between PT/LBW and lower wealth in adulthood. Nevertheless, studies have revealed inconsistent findings so far.

OBJECTIVE: To systematically investigate whether PT/LBW is associated with markers of adulthood wealth.

DATA SOURCES: We searched Medline, PubMed, PsycINFO, Web of Science, and Embase.

STUDY SELECTION: Prospective longitudinal and registry studies containing reports on selected wealth-related outcomes in PT/LBW-born adults compared with term-born controls.

DATA EXTRACTION: Two independent reviewers extracted data on educational qualifications, employment rates, social benefits, and independent living.

RESULTS: Of 1347 articles screened, 23 studies met the inclusion criteria. PT/LBW was associated with decreased likelihood of attainment of higher education qualifications (odds ratio [OR] = 0.74; 95% confidence interval [CI] = 0.69–0.80), lower employment rate (OR = 0.83; 95% CI = 0.74–0.92), and increased likelihood of receiving social benefits (OR = 1.25; 95% CI = 1.09–1.42). A dose-response relationship according to gestational age was only found for education qualifications. PT/LBW-born adults did not differ significantly from those born at term in independent living.

LIMITATIONS: There was high heterogeneity between studies. There were unequal numbers of studies from different regions in the world.

CONCLUSIONS: PT/LBW is associated with lower educational qualifications, decreased rate of employment, and an increased rate of receipt of social benefits in adulthood. Low educational qualifications were most prevalent in those born very preterm and consistent across geographic regions. However, the findings are less clear for independent living.

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Dr Bilgin was involved in the conception of the study, conducted the data collection and analyses, and drafted the manuscript; Dr Mendonca was involved in the conception of the study and conducted the data collection; Dr Wolke conceptualized and designed the study and supervised the study; and all authors reviewed and revised the manuscript and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Approximately 11.1% of children are born preterm (<37 weeks' gestation) worldwide, and 8.6% of all children born preterm are born in developed countries.[1] Improvements in neonatal care, such as the use of assisted ventilation, the introduction of advanced technology[2,3] and changing attitudes toward intensive care[4] have resulted in marked increases in the survival rate of preterm infants. Across the lifespan, preterm birth is associated with an increased risk of disability,[5,6] neurocognitive impairment,[7–10] learning difficulties,[7,10] and mental health problems,[11–13] and the association is stronger in those who were born very preterm (VPT).[7,14,15] Generally, disability, neurocognitive impairment, and mental health disorders in childhood and early adulthood have been associated with markers of reduced wealth such as attainment of poorer educational qualifications, lower employment, and increased receipt of social benefits in young adults in adulthood.[16]

Large, registry-based studies from Scandinavian countries have contained further documentation that preterm birth may not be only associated with adverse functional outcome but with a decrease in markers of wealth across adulthood, such as lower levels of education and lower rates of employment, education, and independent living and higher rates of receiving social security benefits compared with those born at term.[15,17–20] This would suggest that apart from increased health care costs,[21] there may be long-term adverse effects on individual wealth and social cost for society. In contrast, few prospective cohort studies have included adult wealth-related outcomes after preterm birth, and inconsistent findings have been produced in these studies.[6,22–25] For example, the results from a cohort study of Canadian extremely low birth weight (LBW) infants revealed no significant differences in the years of education between those born preterm and those born at term,[6,24,25] whereas the results of other studies from the United Kingdom and United States revealed that preterm birth was associated with a decrease in educational qualifications.[22,23] Regarding employment, Saigal et al[6,25] found similar rates among those born preterm and those born at term in young adulthood, although those born at an extremely LBW were less likely to be employed in middle adulthood. Thus, there are variations in findings, and differences in markers of wealth may depend on the degree of prematurity, region in the world, study design, or length of follow-up.

Our aim in this study was to systematically investigate if preterm birth and/or low birth weight (PT/LBW) is associated with a decrease in markers of wealth in adulthood as assessed through educational qualifications attained, employment rate, receiving social benefits, and independent living, while assessing whether there is a dose-response effect according to gestational age at birth (VPT: <32 weeks' gestation or moderate-to-late preterm [MLPT]: 32–36 weeks' gestation at birth), moderation by geographical region (Europe, North America, and Australasia), study type (registry or cohort), and assessment age (middle or young adulthood).

METHODS

This meta-analysis was registered with the PROSPERO International prospective register of systematic reviews with the following number: CRD42017064788. This meta-analysis was conducted in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[26]

Study Selection Criteria

Prospective longitudinal and registry studies were eligible for this meta-analysis. Studies were included in the analysis according to 5 criteria. First, articles should contain reports on at least 1 of the following variables assessing wealth: higher education qualifications (postsecondary education [ie, qualifications you can attain at a university or other higher education institutions]), employment (full-time or part-time employment), receiving social benefits (government social welfare subsidies), and independent living (not living in parents' house). Second, studies had to include a term healthy control group. Third, studies had to include participants with a mean age of ≥18 years at the time of outcome assessment. Fourth, enough statistical information (means, SDs, frequencies) should be reported in the articles or provided by authors after contacting them to enable computing effect sizes. Last, the articles had to be in either English or in German. Studies not fulfilling these criteria were excluded (Fig 1).

Search Strategy

A literature search was conducted for longitudinal studies of markers of wealth in adults who were born preterm (<37 weeks' gestation) or LBW (<2500 g at birth), published between January 1980 and May 2017. The article search was finalized on May 15, 2017. The following electronic databases were searched: Medline, PubMed, PsycINFO, Web of Science, and Embase. The keywords used were as follows: (preterm OR low birth weight OR prematur*) AND (socioeconomic status OR wealth OR employment OR academic OR education OR benefits OR independent) AND (adult*).

The Medline search yielded 248 articles, PubMed yielded 324 articles,

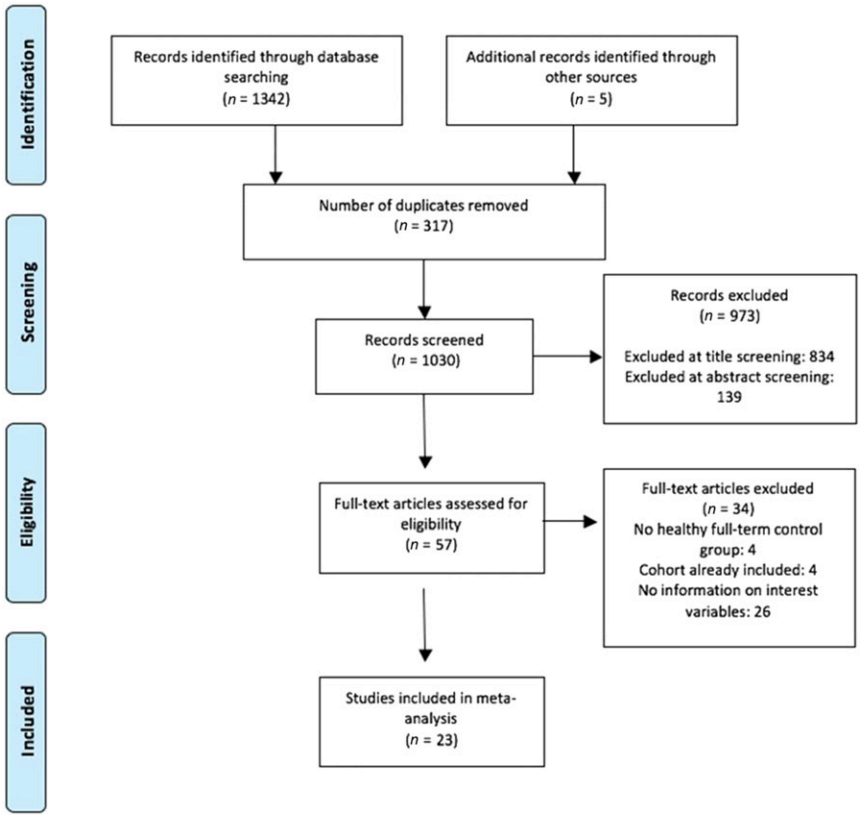

FIGURE 1
Flow diagram.

PsycINFO yielded 106 articles, Web of Science yielded 357 articles, and Embase yielded 307 articles. Furthermore, 5 articles were found from bibliography search. Overall, 1347 articles were included in the literature search. In total, 317 duplicates were removed from the search. Overall, the final literature search included 1030 articles (see Fig 1). After the title screening, 196 articles were left for abstract screening. In total, 139 articles were excluded on the basis of the abstract only. We reviewed the full text of the remaining 57 articles according to the inclusion criteria, and 34 articles were excluded. In some cases, multiple reports were published on the same cohort assessed at different time periods in adulthood.[6,24,27] To avoid inappropriate double-counting of participants that may have influenced study weighting, only 1 study was included in any meta-analysis. When a choice was required, those studies with the best profile (for example, the largest sample sizes and the broadest concept coverage) were selected for inclusion in meta-analysis. Nevertheless, 2 studies[6,25] were included from the same Canadian sample since Saigal et al[25] reported on independent living, which was not available in the largest sample size study from the same cohort.[6] Moreover, the authors of 1 study reported on 2 samples[22] resulting in a total of 23 articles with 23 samples being included in the meta-analysis (Table 1). The article selection process was performed by AB and MM independently. The overall agreement in the selection of articles according to the predefined criteria was Cohen's κ 0.84 at the abstract selection stage and 0.90 at the full-text retrieval stage. The discrepancies in 4 articles were discussed and mutually resolved by the coders and D.W.

Quality Assessment

The Newcastle-Ottawa Scale[42] was used to assess the quality of studies referring to selection, comparability, and outcome or exposure for cohort studies (see Supplemental Table 4). Scores in this scale could range from 0 to 9, with higher scores indicating higher quality. Studies were rated by 2 independent coders, and agreement for the overall rating for each study was found to be high (κ = 0.86). The overall ratings of the studies ranged from 6 to 9 (mean = 7.5; SD = 0.7), indicating overall high quality.

Data Extraction

Eligible studies were reviewed to extract the wealth data. When available, information on the comparison of PT/LBW and term groups was extracted directly from the article. Authors that reported on LBW and preterm birth were grouped into the same category because infants with LBW were mostly also born preterm. Data were provided in studies in different formats: sample size with means and SDs, or frequencies. When any of this information was unavailable, it was requested from the authors. In cases in which the researchers reported the statistical information according to different gestational age subgroups,[15,17,19,20] the data were combined into 3 groups by degree of prematurity: (1) VPT (<32 weeks), (2) MLPT (32–36 weeks), and (3) term (>36 weeks). Nevertheless, Männistö et al[39] reported on an early preterm (<34 weeks) subgroup overlapping with MLPT subgroup. In this case, we excluded this statistical information from the analysis. Categorical information regarding the degree of prematurity (VPT or MLPT), geographical setting (Australasia, Europe, or North America), the type of study (cohort or registry), and assessment age in adulthood (young adulthood ≤30 years or middle adulthood >30 years) was extracted from the articles

TABLE 1 Summary of the Studies Included in the Analysis of Wealth in Adulthood After PT/LBW (≥18 Years)

Author(s), (y)	Country	Y of Birth	No. Participants		Male *n* (%)		Outcome Assessment Age (Mean or Range)	Degree of Prematurity	Registry or Cohort (Name)	Measured Variable(s)
			PT	Term	PT	Term				
Allin et al,[28] (2006)	United Kingdom	1979–1981	108	67	51 (47.2)	39 (51.2)	18–19 y	VPT	Cohort: NA	Higher education qualifications, employment
Basten et al,[22] (2015) BCS	United Kingdom	1958–1970	320	6378	158 (49.4)	3045 (47.7)	42 y	VPT, MLPT	Cohort: British Cohort Study	Higher education qualifications, employment
Basten et al,[22] (2015) NCDS	United Kingdom	1958–1970	403	8170	202 (50.1)	4054 (49.6)	42 y	VPT, MLPT	Cohort: National Child Development Study	Higher education qualifications, employment
Båtsvik et al,[29] (2015)	Norway	1982–1985	37	46	19 (51.4)	25 (54.4)	24 y	EPT	Cohort: NA	Higher education qualifications, employment, benefits, independent living
Baumann et al,[30] (2016)	Germany	1985–1986	260	229	118 (45.3)	130 (53.7)	26 y	VPT and/ orVLBW	Cohort: Bavarian Longitudinal Study	Employment, benefits, independent living
Cooke,[31] (2004)	United Kingdom	1980–1983	79	71	35 (44.3)	30 (42.3)	20 y	PT	Cohort: NA	Higher education qualifications, employment
Dalziel et al,[32] (2007)	New Zealand	1969–1974	126	66	66 (52.3)	33 (50)	31 y	PT	Cohort: Auckland Steroid Trial	Higher education qualifications
Darlow et al,[33] (2013)	New Zealand	1986	230	69	104 (45.2)	33 (47.8)	22–23 y	VLBW	Cohort: NA	Higher education qualifications, employment, benefits
D'Onofrio et al,[15] (2013)	Sweden	1973–2008	154 322	3 146 386	85 195 (55.2)	1 618 442 (51.4)	38 y	VPT and MLPT	Registry	Higher education qualifications, benefits
Hack et al,[23] (2002)	United States	1977–1979	242	233	116 (48)	108 (46)	20 y	VLBW	Cohort: NA	Higher education qualifications
Heinonen et al,[34] (2013)	Finland	1934–1944	486	8507	262 (53.9)	4506 (53)	56–66 y	MLPT	Cohort: Helsinki Birth Cohort Study	Higher education qualifications, employment
Kajantie et al,[35] (2008)	Finland	1978–1985	162	188	68 (42)	75 (39.9)	22.3 y	VLBW	Cohort: Helsinki Study of Very Low Birth Wt Adults	Independent living
Kroll et al,[36] (2017)	United Kingdom	1979–1984	122	89	76(62)	42(47)	31.2 y	VPT	Cohort: NA	Higher education qualifications, employment
Lærum et al,[37] (2017)	Norway	1986–1988	44	81	21 (48)	38 (47)	26 y	VLBW	Cohort: NA	Higher education qualifications, employment, social benefits
Lefebvre et al,[38] (2005)	Canada	1976–1981	69	44	29 (42)	15 (34.1)	18 y	ELBW	Cohort: NA	Higher education qualifications
Lindström et al,[17] (2007)	Sweden	1973–1979	90 654	431 656	49 242 (54.3)	220 310 (51)	23–29 y	VPT and MLPT	Registry	Higher education qualifications, employment, benefits, independent living
Männistö et al,[39] (2015)	Finland	1985–1989	397	356	189 (47.6)	170 (47.8)	23.2 y	VPT and MLPT	Cohort: ESTER	Independent living

TABLE 1 Continued

Author(s), (y)	Country	Y of Birth	No. Participants		Male *n* (%)		Outcome Assessment Age (Mean or Range)	Degree of Prematurity	Registry or Cohort (Name)	Measured Variable(s)
			PT	Term	PT	Term				
Mathiasen et al,[18] (2009)	Denmark	1974–1976	1422	192 233	736 (51.8)	98 240 (51.1)	27–29 y	VPT	Registry	Higher education qualifications, employment, benefits, independent living
Moster et al,[19] (2008)	Norway	1967–1983	39 465	828 227	21 715 (55)	421 568 (50.9)	19–35 y	VPT and MLPT	Registry	Higher education qualifications, employment, benefits
Odberg and Elgen,[40] (2011)	Norway	1986–1988	134	135	61 (54)	64 (53)	18 y 11 mo	<2000 g	Cohort	Higher education qualifications
Saigal et al,[6] (2016)[a]	Canada	1977–1982	100	89	39 (39.0)	33 (37.1)	32.3 y	ELBW	Cohort: McMaster ELBW Cohort	Higher education qualifications, employment
Saigal et al,[25] (2006)[a]	Canada	1977–1982	149	133	67 (45)	60 (45)	23.5 y	ELBW	Cohort: McMaster ELBW Cohort	Independent living
Swamy et al,[20] (2008)	Norway	1967–1988	64 956	1 648 496	33 754 (60)	566 339 (33.7)	NA	VPT and MLPT	Registry	Higher education qualifications
Winstanley et al,[41] (2015)[b]	United Kingdom	NA	11 592	51 460	3554 (30.7)	8038 (69.3)	31.4 y	PT	Cohort: NA	Employment

ELBW = <1000 g; LBW = <2500 g; MLPT = 32–36 wk; VLBW = <1500 g; VPT = <32 wk gestation. NA, not available.

[a] Same cohort reporting on different age groups. Saigal et al[25] was included in the analysis for independent living.

[b] Please note that in this study, preterm birth was self-reported in an online survey.

(Table 1). The categorization of these variables was completed by A.B. under the supervision of D.W., the senior author.

Data Analysis

Analysis was conducted with Comprehensive Meta-Analysis version 2 software.[43] Mean effect sizes were calculated with the Comprehensive Meta-Analysis software when studies reported group differences at different time points. Because the eligible studies varied in many aspects, differences in the outcomes between PT/LBW and term adults were assessed by using random effects meta-analyses, an approach that assumes the studies included in the analyses are random samples from a larger population of studies and likely to exhibit different effect sizes.[44] We calculated odds ratios (ORs) and their confidence intervals (CIs). Heterogeneity of studies was assessed with Cochran *Q* test and Higgins I^2. Subgroup analyses were conducted with the following 4 variables: degree of prematurity, type of study, geographical setting, and assessment age in adulthood (young versus middle adulthood).

Publication bias analysis was assessed by using 3 strategies. First, the trim and fill procedure was used to examine the symmetry of effect sizes plotted by the inverse of the SE.[45] Ideally, the effect sizes should mirror one another on either side of the mean. Second, the Begg and Mazumdar[46] rank correlation test was used to examine the likelihood of bias in favor of small sample size studies. Nonsignificance of correlation indicates no publication bias. Last, Egger et al[47] examined with their test whether publication bias related to the direction of study findings. The intercept value provided by this test reveals the level of funnel plot asymmetry from the standard precision.

In the current meta-analysis, we decided to combine preterm and LBW into 1 group. Because it was essential to demonstrate that the findings of the meta-analysis were not dependent on this decision, a sensitivity analysis was undertaken in which we repeated the analysis just for studies reported on preterm excluding the studies that contained reports on LBW only.

RESULTS

The 23 samples and 23 studies of adulthood wealth-related outcomes represented a total of 5 917 101 participants, 271 767 of whom were born PT/LBW and 5 645 334 were born at term. Seven (30.4%) of the samples contained reports on birth weight, 15 (65.2%) contained reports on gestational age, and 1 study[30] contained a report on both birth weight and gestational age. Sample sizes for the PT/LBW group ranged from 35 to 114 890 individuals; for the term group, the sample sizes ranged from 30 to 3 146 386 individuals. Mean birth weight was 1618.5 g (SD = 717.4) for PT/LBW participants and 3494.9 g (SD = 189.9) for term participants. The mean gestational age of the PT/LBW children was 30.4 weeks (SD = 2.8 weeks) compared with 39.6 weeks (SD = 1.1 weeks) for the term comparisons. The age of participants at assessment ranged from 18 to 66 years. Ten (43.8%) of the samples included participants ≤29 years and the other 13 (56.2%) samples included participants >29 years. Eighteen of the studies contained reports on higher education qualifications, 15 contained reports on employment, 7 contained reports on receiving social benefits, and 6 contained reports on independent living. The majority of the studies were from Europe (N = 17). There were few studies from North America (N = 4) and Australasia (N = 2) and no studies from elsewhere in the world. Of the articles included, 18 (78.3%) contained reports on a cohort sample, and the remaining 5 (21.7%) contained reports on registry samples.[15,17]

Differences in Higher Education Qualifications Between Adults Born PT/LBW and at Term

There was a significant negative association between PT/LBW and achievement of higher education qualifications (OR = 0.74; 95% CI = 0.69–0.80), indicating that preterm birth was associated with a decrease in the likelihood of completing education beyond high school (Table 2). Heterogeneity analysis indicated significant and high variation in education effects between studies (Q = 111.63; I^2 = 85, P < .001). Subgroup analysis according to the degree of prematurity revealed a significant difference between the 2 groups (Q = 7.48; I^2 = 86.6, P < .05) in which both VPT (OR = 0.60; 95% CI = 0.48–0.74) and MLPT (OR = 0.82; 95% CI = 0.78–0.85) decreased the likelihood of attainment of higher education qualifications (Supplemental Fig 2). Comparison of the region of the studies indicated that in all 3 regions, (Australasia [OR = 0.59; 95% CI = 0.26–1.32], Europe [OR = 0.76; 95% CI = 0.71–-0.82], and North America [OR = 0.66; 95% CI = 0.49–-0.90]) preterm birth decreased the likelihood of achieving higher education qualifications in adulthood (Supplemental Fig 3). This association was significant in both cohort and registry studies, respectively (OR = 0.59; 95% CI = 0.48–0.74 and OR = 0.79; 95% CI = 0.74–0.85). When comparing young and middle-aged adults, the PT/LBW group was less likely to achieve higher education qualifications compared with term group both in young adulthood (OR = 0.61; 95% CI = 0.49–0.77) and middle adulthood (OR = 0.77; 95% CI = 0.72–0.84).

Differences in Employment Between Adults Born PT/LBW and at Term

The combined OR of the employment rate was 0.83 (95% CI = 0.74–0.92; P < .001), indicating that preterm birth was associated with a decrease in the likelihood of being employed in adulthood (Table 2). Heterogeneity analysis indicated significant and high variation in employment effects between studies (Q = 144.45; I^2 = 90, P < .001). Subgroup analysis revealed that both the VPT and MLPT groups (OR = 0.87; 95% CI = 0.76–0.99) were less likely to be employed in adulthood compared with the term group (OR = 0.81; 95% CI = 0.70–0.95), although there was no significant difference between the VPT and MLPT groups. In comparing the regions, studies from both Europe (OR = 0.84; 95% CI = 0.75–0.93) and North America (OR = 0.37; 95% CI = 0.15–0.93) revealed that the PT/LBW group had a decreased likelihood of employment in adulthood; nevertheless, this association was not significant in Australasia. There was a significant association between PT/LBW and employment in both cohort (OR = 0.76; 95% CI = 0.61–0.95) and registry studies (OR = 0.91; 95% CI = 0.86–0.97). When comparing young and middle-aged adults, those born PT/LBW were less likely to be employed compared with those born at term only in middle adulthood (OR = 0.76; 95% CI = 0.62–0.93).

Differences in Social Benefits Between Adults Born PT/LBW and at Term

There was a significant positive association between preterm birth and receiving social benefits (OR = 1.25; 95% CI = 1.09–1.42), suggesting that preterm birth was associated with an increase in the likelihood of

TABLE 2 Associations Between PT/LBW and Higher Education Qualifications and Employment in Adulthood

	Data Points	OR	95% CI Lower Bound	95% CI Upper Bound	Cochran *Q* Test	I^2	Test for Heterogeneity (*P*)
Higher education qualifications[a]							
All studies	18	0.74	0.69	0.80	111.63	85	<.001
Degree of prematurity[b]							
MLPT (32–36 wk GA)	10	0.82	0.78	0.85	40.88	78	<.001
VPT (<32 wk GA)	15	0.60	0.48	0.74	263.05	95	<.001
Age							
Young adulthood (18–29 y)	9	0.61	0.49	0.77	14.01	43	.08
Middle adulthood (≥30 y)	9	0.77	0.72	0.84	89.60	91	<.001
Study type							
Cohort	14	0.59	0.48	0.72	27.88	53	.01
Registry	4	0.79	0.74	0.85	73.72	96	<.001
Region							
Australasia	2	0.59	0.26	1.32	2.98	66	.08
Europe	13	0.76	0.71	0.82	99.23	88	<.001
North America	3	0.66	0.49	0.90	0.84	0	.66
Employment							
All studies	15	0.83	0.74	0.92	144.45	90	<.001
Degree of prematurity[b]							
MLPT (32–36 wk GA)	7	0.87	0.76	0.99	119.68	95	<.001
VPT (<32 wk GA)	10	0.81	0.70	0.95	27.61	67	.001
Age							
Young adulthood (18–29 y)	8	0.86	0.73	1.02	21.69	68	.003
Middle adulthood (≥30 y)	7	0.76	0.62	0.93	122.10	95	<.001
Study type							
Cohort	12	0.76	0.61	0.95	24.36	55	.01
Registry	3	0.91	0.86	0.97	12.59	84	.002
Region							
Australasia	1	0.70	0.38	1.28	—	—	—
Europe	13	0.84	0.75	0.93	140.21	91	<.001
North America	1	0.37	0.15	0.93	—	—	—

GA, gestational age; —, not applicable.

[a] Higher education qualifications refer to attainment of qualifications beyond high school.

[b] Please note that the number of data points are higher in the degree of prematurity analysis since some studies reported on >1 degree of prematurity.

receiving social benefits (Table 3). Heterogeneity analysis indicated significant and high variation in benefit usage effects between studies (Q = 148.92; I^2 = 96, P < .001). Subgroup analysis according to degree of prematurity revealed that adults were more likely to receive benefits both in the VPT group (OR = 1.78; 95% CI = 1.09–2.91) and MLPT group (OR = 1.16; 95% CI = 1.14–1.19); however, the difference between the VPT and MLPT groups was not significant. In comparing the region of the studies, studies from both Australasia (OR = 2.67; 95% CI = 1.51–4.75) and Europe (OR = 1.20; 95% CI = 1.05–1.37) revealed that adults born PT/LBW were more likely to receive benefits in comparison with term born. No studies from North America contained reports on receiving benefits after preterm birth. In comparing the studies according to study type, preterm adults were more likely to receive benefits in both cohort (OR = 3.98; 95% CI = 1.39–11.37) and registry studies (OR = 1.18; 95% CI = 1.04–1.35) in comparison with term adults. When comparing young and middle-aged adults, those born PT/LBW were more likely to receive benefits compared with those born at term in both young adulthood (OR = 2.12; 95% CI = 1.00–4.48) and middle adulthood (OR = 1.14; 95% CI = 1.05–1.35).

Differences in Independent Living Between Adults Born PT/LBW and at Term

The combined mean OR of independent living was 0.78 (95% CI = 0.60–1.01), indicating no difference in independent living away from their parents between PT/LBW and term comparison adults (Table 3). Heterogeneity analysis indicated significant and high variation in independent living effects between studies (Q = 31.13; I^2 = 80.72, P < .001). Subgroup analyses according to the degree of prematurity and region showed no significant difference between preterm and term comparison adults in independent living. However, PT/LBW adults were less likely to live independently according to cohort studies (OR = 0.59; 95% CI = 0.44–0.79) but more likely to live independently according to registry studies (OR = 1.09; 95% CI = 1.01–1.18).

TABLE 3 Associations Between PT/LBW and Benefits and Independent Living in Adulthood

	Data Points	OR	95% CI Lower Bound	95% CI Upper Bound	Cochran *Q* Test	I^2	Test for Heterogeneity (*P*)
Social benefits							
All studies	7	1.25	1.09	1.42	148.92	96	<.001
Degree of prematurity[a]							
MLPT (32–36 wk GA)	3	1.16	1.14	1.19	2.93	32	.23
VPT (<32 wk GA)	7	1.78	1.09	2.91	236.91	97	<.001
Age							
Young adulthood (18–29 y)	5	2.12	1.00	4.48	116.89	97	<.001
Middle adulthood (≥30 y)	2	1.14	1.05	1.24	24.77	96	<.001
Study type							
Cohort	3	3.98	1.39	11.37	2.77	28	.25
Registry	4	1.18	1.04	1.35	133.23	98	<.001
Region							
Australasia	1	2.67	1.51	4.75	—	—	—
Europe	6	1.20	1.05	1.37	139.98	96	<.001
North America	0	—	—	—	—	—	—
Independent living							
All studies	7	0.78	0.60	1.01	31.13	80.72	<.001
Degree of prematurity[a]							
MLPT (32–36 wk GA)	2	0.73	0.30	1.77	8.49	88	.004
VPT (<32 wk GA)	6	0.84	0.62	1.15	26.89	81	.27
Age[b]							
Young adulthood (18–29 y)	—	—	—	—	—	—	—
Middle adulthood (≥30 y)	—	—	—	—	—	—	—
Study type							
Cohort	5	0.59	0.44	0.79	5.11	22	.28
Registry	2	1.09	1.01	1.18	1.37	27	.24
Region							
Australasia	0	—	—	—	—	—	—
Europe	6	0.81	0.62	1.07	26.49	81.00	<.001
North America	1	0.66	0.41	1.06	—	—	—

GA, gestational age; —, not applicable.

[a] Please note that the number of data points are higher in the degree of prematurity analysis because some studies contained reports on >1 degree of prematurity.

[b] Please note that all studies that contained reports on independent living had young adult participants.

Publication Bias

Under the random effects model, the point estimate (95% CI) for the combined studies is 0.75 (0.70–0.80) for higher education qualifications and 0.82 (0.74–0.92) for employment. With the use of trim and fill, these values remained unchanged for both higher education qualifications and employment, indicating no publication bias. The Begg and Mazumdar[46] rank correlation and Egger et al's[47] test were not statistically significant for both employment and higher education qualifications, indicating no evidence of publication bias.

Under the random effects model, the point estimate (95% CI) for the combined studies is 1.11 (1.10–1.13) for receiving social benefits. With the use of trim and fill, the imputed point estimate changed to 1.18 (1.04–1.35), indicating publication bias. On the other hand, the Begg and Mazumdar[46] rank correlation and Egger's et al[47] test were not statistically significant, indicating no evidence of publication bias.

Under the random effects model, the point estimate (95% CI) for the combined studies is 0.78 (0.60–1.01) for independent living. With the use of trim and fill, these values remained unchanged, indicating no publication bias. The Begg and Mazumdar[46] rank correlation was not statistically significant; however, Egger et al's[47] test was statistically significant (*P* = .01), indicating publication bias. However, Egger et al's[47] test has low power when few studies are included in the analysis and when there is high heterogeneity between studies.[48,49]

Sensitivity Analysis

Because the current meta-analysis included a mixture of studies containing reports on birth weight and gestational age, we repeated the meta-analysis excluding the studies that contained reports on birth weight to check whether this altered the results.[50] Results remained the same when the studies containing reports on birth weight were removed from the analysis. Preterm born adults were less likely to attain higher education qualifications (OR = 0.77; 95% CI = 0.72–0.83), be employed (OR = 0.84; 95% CI = 0.75–0.93), and more likely to receive social benefits (OR = 1.19; 95% CI = 1.04–1.36) in comparison

with term-born adults. There was no significant difference between the 2 groups in terms of the likelihood of independent living (OR = 0.81; 95% CI = 0.61–1.06).

DISCUSSION

Our findings revealed that adults born PT/LBW are less likely to achieve higher education qualifications, less likely to be employed, and they are more likely to receive social benefits in comparison with those born at term. On the other hand, PT/LBW- and term-born adults were similar in the likelihood of independent living.

With respect to study type, the results of cohort studies revealed generally poorer outcomes in higher education qualifications and employment rates for PT/LBW-born adults than registry studies, along with increased rate of receiving social benefits. As cohort studies are prone to selective dropout (ie, participants with the worst social conditions and problems are more likely to drop out),[51,52] cohort studies would have been expected to contain reports on less problems in comparison with registry studies. This difference according to study type may be related to the fact that all registry studies were from Scandinavian countries, where inclusive education, employment rates, and educational qualifications could be relatively high compared with other countries.[53] It could also be related to the fact that the majority of cohort studies included VPT or very low birth weight (VLBW) individuals, whereas registry studies included the full range of preterm birth. With respect to region, the inverse association between preterm birth and higher education qualifications in adulthood was more pronounced in Australasia and North America in comparison with Europe. This finding could be due to having less of a social care network for those born preterm in these regions than Europe.[54] On the other hand, it could also be a methodological issue due to having registry studies in Europe but not in other regions.

Despite poorer education, being less likely to be employed, and receiving social benefits, preterm-born adults were as likely to live independently as term-born adults. We found that this was particularly evident in registry studies, which indicates that welfare and cultural practices might have an influence on this outcome. To illustrate, in northern European countries, it is socially expected for young people to leave home, and the state usually supports this transition.[55] However, it should be noted that cohort studies did report less independent living of those born PT/LBW. Thus, cohort studies may provide more sensitive measurement of independent living because they usually include detailed information about the living arrangements, whereas registry studies may only contain reports based on a registered address that might not indicate where the individual actually lives.[30]

The primary and subgroup analyses allow for interpretation of the evidence by using the Hill[56] Framework (a tool to assess for causality between 2 variables) on the basis of the following: the temporal relationship of the association, strength and consistency of the association, presence of a dose-response relationship, plausibility, and whether an alternate explanation for the associations is possible.

With respect to temporality, longitudinal prospective studies showed a significant association between PT/LBW and markers of adulthood wealth, particularly for higher education qualifications, employment, and social benefits. Thus, there is evidence of a temporal relationship showing PT/LBW preceded later consequences regarding economic functioning.

The magnitude of the associations was generally small and diverged depending on the study type, degree of prematurity, region, and participant age. To illustrate, the results of cohort studies revealed more negative associations between being born PT/LBW and higher education qualifications and employment in comparison with registry-based studies. Despite some variability, being born PT/LBW was found to significantly decrease the likelihood of attainment of higher education qualifications and employment and increase the likelihood of receiving social benefits. These findings suggest robust associations between being born PT/LBW and markers of adulthood wealth.

Consistency of the associations between being born PT/LBW and a decrease in markers of adulthood wealth was demonstrated in the estimated effect sizes across studies. The significant association was consistent across different geographic regions, degree of prematurity and study type for higher education qualifications, and employment. The significant association was consistent across different regions for social benefits. Inconsistent associations were observed for independent living, and it is possible that publication bias or assessment method affected the results for independent living.

With respect to dose-response relationship, available evidence suggests that among those born preterm, being born before 32 weeks (VPT) is specifically associated with impairments in multiple areas of development.[7,57] Similarly, we suggest a dose-response relationship between being born PT/LBW and markers of adulthood wealth, in particular for higher education qualifications. An increase in the degree of prematurity (ie, decrease in gestational age) resulted in the lowest point of estimates for higher education qualifications and employment. To illustrate, VPT infants had significantly lower likelihood of attainment of higher education qualifications in

comparison with MLPT infants. Although the difference between VPT and MLPT infants in the likelihood of employment was not significant, the point estimate for VPT infants was lower than MLPT infants. VPT resulted in the highest point of estimates for receiving social benefits, although the difference between VPT and MLPT was not statistically significant.

In infants born preterm, the normal processes of intrauterine brain development are altered or impaired during the second half of gestation (20–40 weeks), with the maturation of cerebral pathways, the formation of synapses, and brain growth being interrupted.[58,59] The severity of these alterations has been associated with neurocognitive deficits in later life.[60,61] Thus, it is plausible that being born PT/LBW would be associated with low employment and educational qualifications in adulthood.

There are alternative explanations for the association between being born PT/LBW and a decrease in markers of wealth in adulthood. One factor related to increased rates of preterm birth is low socioeconomic status of the mother, which has been consistently reported in several countries such as United States,[62] Sweden,[63] Finland,[64] or United Kingdom.[65] Social disadvantage has been shown to be an equally important factor in explaining the cognitive deficits as VPT birth.[66,67] The impact of gestational age on cognitive deficits decreases after controlling for social disadvantage while growing up,[68] and the effects of social disadvantage and VPT have been shown to be additive.[67] Nevertheless, some studies included in the meta-analysis reported an association between PT/LBW and decreased employment[30] and educational qualification rates[17] even after controlling for the impact of socioeconomic status of the mother.

Using the above-mentioned criteria, we can conclude that there is "convincing evidence" for an association between PT/LBW and decreased likelihood of higher education qualifications and employment. This evidence is based on a substantial number of cohort and registry studies identified in this meta-analysis, including prospective cohort studies of sufficient size, duration, and quality revealing consistent effect sizes. We conclude that probable evidence of an association exists between PT/LBW and increased likelihood of receiving social benefits. This evidence is mainly based on findings from registry studies and 2 cohort studies. More studies are needed to support these tentative associations. Further research with more fine-graded assessment is needed to better examine if any associations exist between PT/LBW and independent living.

There are some limitations of the current meta-analysis. There were too few studies from North America and Australasia and no studies from other regions. These would be needed to understand the impact of PT/LBW on wealth in all regions of the world. Information on the disability of the participants was also not available for the majority of studies and thus could not be considered as a moderator in our analysis. Therefore, it could not be assessed whether disability accounted for the association between PT/LBW and wealth-related outcomes. It is essential that future researchers report on disabilities in individuals born with PT/LBW when reporting on adulthood wealth-related outcomes. Moreover, the heterogeneity was high, indicating considerable variation between studies. This might arise from incorporating cohort and registry studies with various sample sizes. To address this possibility, we used a random-effects model in the analysis and conducted moderator analyses. Nevertheless, our moderator analysis explained only some of the heterogeneity. Thus, the findings from the current study should be interpreted with caution, and the analysis should be repeated when more adulthood data becomes available from the extremely preterm cohort studies.[69,70] We were unable to include income as an outcome measure since the definition of low income does differ substantially according to overall distribution of income in each country and reference norms were not available. It was only possible to focus on higher education qualifications among the levels of education because this was the most consistently reported outcome.

CONCLUSIONS

There is evidence that PT/LBW is associated with decreased rates of educational qualifications and employment as well as increased rate of social benefits in adulthood. Although the magnitude of these associations was small in general, they were particularly strong in VPT- or VLBW-born adults for education qualifications and were consistent across geographic regions. However, the findings are less clear for independent living, which may be related to measurement or cultural practices and support. Future researchers should identify the major risks and, in particular, protective and resiliency factors related to wealth among preterm individuals to improve support and design appropriate interventions to decrease the economic disadvantages of survivors of PT/LBW.

ABBREVIATIONS

CI: confidence interval
LBW: low birth weight
MLPT: moderate-to-late preterm
OR: odds ratio
PT/LBW: preterm birth and/or low birth weight
VLBW: very low birth weight
VPT: very preterm

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